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A CASE OF ANEURYSMAL DISEASE, WITH OBSERVATIONS.

By CECIL F. BEADLES.

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(Plates III. and IV.)

Summary.—Multiple small aneurysmal dilatations on the larger arteries at the base of the brain affected with syphilitic endarteritis, syphilitic deposits and softenings in both cerebral hemispheres, symmetrical aneurysms at the bifurcation of both common carotid arteries, great localised dilatation with thrombosis of both coronary arteries, in a patient presenting the clinical symptoms of general paralysis.

History.—J. J., a married man, æt. 38, tailor by occupation, was admitted to Claybury Asylum on 10th February 1903, on the following medical certificates:—"(*a*) Prematurely aged, appeared to be suffering from softening of the brain and subject to what may be described as melancholic stupor. Is certainly irresponsible and unfit to be at large. (*b*) Wife states: during the night he will use obscene language, calling me a whore. This is unnatural of him. Neglects his person, and is sometimes violent."

Particulars obtained from the wife are to the effect that the patient's mind had been affected for twelve months, but he had not before been confined in an asylum. The only cause that could be attributed was ill-health. He had had rheumatic gout, and ten years ago had influenza. Was steady in habits. An aunt on father's side had been insane. Married for fourteen years, and had two children (twins), æt. 13 years. The first sign of mental disorder noticed was loss of memory; had been violent towards her; forgot his work. Of late he had been the reverse of cheerful. He could sleep at any time, and his appetite had been very good ever since his illness began.

Present State on Admission, by Dr. Pugh.—Lipoma on both wrists. Tongue flabby, finely tremulous. Heart sounds clear. Breathing vesicular, no accompaniments. Pupils unequal, left contracted, light reflexes sluggish. Knee-jerks brisk, and plantar reflexes exaggerated. No paralysis of limbs and no sign of paresis of face, but gait unsteady and muscular co-ordination impaired. Speech slurred and indistinct, and power of articulation impaired. Lies in bed in supine position. Has a fatuous expression, is restless, irritable, and bad tempered. Mental reaction slow; answers questions in a hesitating manner; ideas slowly formed, and are very confused. Expresses delusions freely; says that "his wife is a wicked woman, that she wanted and attempted to kill him." Mistakes identity of persons. Memory much

[1] I am greatly indebted to Dr. G. A. Watson in connection with this case; first for allowing me to use his post-mortem notes, and secondly for assistance in the preparation and examination of the microscopical sections. I have also to thank Dr. Mott for placing the material at my disposal, and Dr. Robert Jones and Dr. Pugh for enabling me to use the clinical notes. For the opinions expressed in this paper, I alone am responsible.

impaired both for recent and remote events, and has no knowledge of time or place.

Further Notes.—*February* 16.—The following note is by Dr. Robert Jones:—"He is suffering from melancholia. He is slow to reply to questions, dull and very reserved. His memory is impaired, and he is unable to give his history. He is very disinclined to speak. Does not take any interest in his surroundings, and is regardless of his personal appearance. He is in poor health and condition. Looks 60 years of age. Denies syphilis." *February* 23.—In a confused and demented state; has no idea of time or place; health poor; gait unsteady; wet and dirty in his habits. *March* 3.—Is in much the same mental state. Physically he is going down hill. Eats and sleeps well. *March* 10.—Continues lost, confused, and very demented. He is in delicate health, and is a well-marked general paralytic. Prematurely old. *May* 12.—Mentally in the same grossly demented state; physically as feeble, very shaky. Wet and dirty in his habits. *June* 12.—Continues in much the same state. The last week he has been very talkative, and has developed grandiose ideas; says he has millions of pounds and a diamond coat. *September* 30.—He has had numerous *seizures* lately, and has been quite helpless in bed. *December* 11.—Continues in much the same lost and demented state; health feeble.

Note by Dr. Jones.—*January* 9, 1904.—"He is suffering from dementia paralytica. He is lost, confused, grandiose, and flippant. He is intensely deluded, thinks he has no end of wealth, that he is a strong man. Memory defective; has no ideas of time or place. Poorly nourished." *February* 21.—Died, the cause of death being returned as "Exhaustion of general paralysis, phthisis, and multiple aneurysms."

Dr. Pugh, who for the most part had this patient under his care, informs me that the patient had all the characters of an ordinary case of general paralysis. There was no seizure immediately preceding death. Throughout the whole time he was under observation no paralysis either of limbs or face was noticeable. The eyes presented no abnormality beyond the inquality of pupils and feeble reaction to light. No defect was detected of any of the special senses. Patient acknowledged having had syphilis and having *drunk* to excess.

Post-mortem by Dr. G. A. Watson.—*External appearances.*—Subject's age is given as 38, but he looks more like 60 years of age. Hair and beard greyish-white. Emaciated. Muscular system poor. Palate high and broad. No arcus senilis. Pupils very irregular in contour; left the largest. Two small scars over sacrum; two or three pigmented scars on legs. No definite external marks of syphilis. No definite scar on penis. Inguinal glands shotty on both sides.

Head.—Skull: diploe well marked, very congested. Dura somewhat thickened. Considerable excess of cerebro-spinal fluid. Pia arachnoid: considerable thickening and much general opacity, partly due to gummatous deposit, most marked in fronto-parietal region; very firm and extensive midline prefrontal adhesions; stripped with some difficulty; marked decortication over upper part of motor area, portions of superior and inferior parietal, temporal and insula. The thickening and opacity, with what was believed to be gummatous deposit, for the most part followed the course of the larger veins down the fissures, and

especially down the whole length of the great anastomotic vein of Trolard. At the base the membrane was not excessively thickened, and did not exhibit any marked degree of this specific deposit. No excess of fluid in subarachnoid space. Vessels: arteries markedly dilated and atheromatous. Many of the vessels show nodular thickenings, and there are several aneurysmal dilatations. The largest is about the size of a haricot bean at anterior end of basilar artery. These will again be referred to more fully. Encephalon: convolutions of about average complexity, gyri rather large; fairly well-marked general wasting, mostly in the prefrontal region, cortical depth markedly diminished, and striation indistinct. White matter very œdematous. In the central white matter of right hemisphere was an area of softening surrounded by some rather dense white putty-like material, believed to be gummatous. Also two or three areas of softening and putty-like deposits of similar character in the central grey ganglia. In the hinder part of the lenticular nucleus of the corpus striatum one of these areas has broken down and produced a cavity, with ragged edges, the size of a hazel-nut. Ventricles considerably dilated; choroid plexuses thickened but not cystic; numerous medium and large granulations on ependyma of lateral, third, and fifth ventricles, and universal large granulations in fourth ventricle uniformally all over the floor. No abnormality was observed about the cerebellum, pons, and medulla on their outer aspects. Cranial nerves apparently normal. Spinal cord not examined. The brain as a whole, on immediate removal from the skull, weighed 1455 grms. On dividing the several parts and allowing the fluid to escape from ventricles, the weights were—right cerebral hemisphere, 555 grms.; left hemisphere, 608 grms.; cerebellum, pons, and medulla, 180 grms. The left cerebral hemisphere stripped of its membranes, 575, giving a loss of 33 grms.

Thyroid gland enlarged; the left lobe contained a cyst the size of a cherry, containing thick glairy brown fluid. Cervical glands not enlarged.

Thoracic organs.—Both lungs presented slight apical adhesions, and on the left side pleuritic adhesions of the posterior border. Bronchial glands enlarged but none caseous or calcareous. Bronchi thickened and contained muco-purulent material. The right apex had a depressed scar with area of fibrosis; several small scattered calcareous nodules in upper lobe and two or three small caseating areas. The left upper lobe riddled with many irregular walled cavities communicating with one another, most numerous near apex, and considerable fibrosis; intervening areas caseating or pneumonic. The lower lobe of both lungs the seat of extensive broncho-pneumonia.

Heart enlarged, especially left side; weight, 378 grms. Left ventricle hypertrophied, muscle firm; auricle somewhat dilated. Right ventricle about natural, contained much white and a little red clot. Tricuspid and pulmonary valves healthy. Flaps of mitral valve slightly thickened at their edges. Cusps of aortic valve considerably thickened, especially the right posterior cusp, behind which the sinus of Valsalva is much dilated. The bulging amounts almost to an aneurysmal dilatation which will contain a full-sized cherry. Coronary arteries: both much dilated. The right on being laid open measures $\frac{3}{4}$ to $\frac{7}{8}$ in. across; its walls contain very extensive atheroma and a little calcareous deposit.

The left coronary is also considerably dilated and its walls similarly diseased; near its commencement it is completely plugged by a dense thrombus for a distance of $\frac{1}{2}$ to $\frac{3}{4}$ in.

Aorta and great vessels.—Wall of arch and thoracic aorta thickened and contained a moderate amount of pearly white fibrosis, generally distributed, for the most part the first stage of atheroma; no calcareous deposit. The abdominal part of the vessel was in a similar condition. Both renal arteries were much thickened. In the arch between the left subclavian and left carotid was a minute pouch pointing in an upward direction. At the bifurcation of each common carotid artery is an aneurysm; that on the right side in the form of a globular swelling, sacculated and of the size of a cherry; that on the left more fusiform, in shape and size resembling a Brazil-nut. The one on the right was placed more particularly at the origin of the external carotid, while that on the left was at the commencement of the internal carotid. Both filled with dense clot. These aneurysmal dilatations of the carotid arteries are shown in the accompanying figure, which is reproduced from a photograph (Plate III., Fig. 1).

Abdominal organs.—Liver weighed 1485 grms.; spleen, 160 grms.; the density of both these organs considerably increased due to fibrosis. Right kidney 140, and left kidney 163 grms.; both very congested, surface mottled and granular, capsule somewhat thickened, density of organs greatly increased, vessels much thickened. The left contained a small cyst. Lining of stomach in a catarrhal condition. Some slight chronic catarrh and patchy congestion of small intestine. Large intestine somewhat dilated throughout, wall thickened, mucosa atrophied, but no evidence of old or recent ulceration. Mesenteric glands slightly enlarged, not caseous or calcareous. Bladder greatly hypertrophied; chronic cystitis.

The immediate cause of death was "cardiac failure, thrombosis of left coronary artery, and tuberculosis of lungs." Other pathological conditions are summarised as, "general paralysis, multiple aneurysms of cerebral vessels, multiple central cerebral softenings and gummata, fibrosis of organs—kidneys, spleen, and liver."

Further Examination of the Cerebral Arteries and the Brain.—Plate IV., Fig. 2, is a representation of the arteries from the base of the brain. Those of the left side, which in the illustration are seen to the right, appear to be slightly more dilated than those of the other side. There is also seen a second anterior communicating vessel between the anterior cerebrals, three-quarters of an inch in front of that at the usual site. Upon the vessels which form the circle of Willis and upon their immediate branches there can be made out at least eight distinct aneurysmal dilatations, as follows:—

1. The largest dilatation is at the anterior extremity of the basilar; it presents the form of a pocket with a thinner broad base in front, becoming more bulged and rounded posteriorly. It measures 1·5 cm. by 1·2 cm. The whole circumference of the vessel is involved. The trunk of the basilar enters the dilatation centrally from behind, and the posterior cerebral arteries pass out from it in front by constricted channels. The two superior cerebellar arteries arise from the sac itself. The wall of the aneurysm is tense and hard, and upon incising it the cavity

Fig. 1. -The arch of the aorta with the two carotid arteries, showing an aneurysm at the bifurcation of both of the latter vessels, involving the origin of the internal carotid arteries.

From a Photograph.

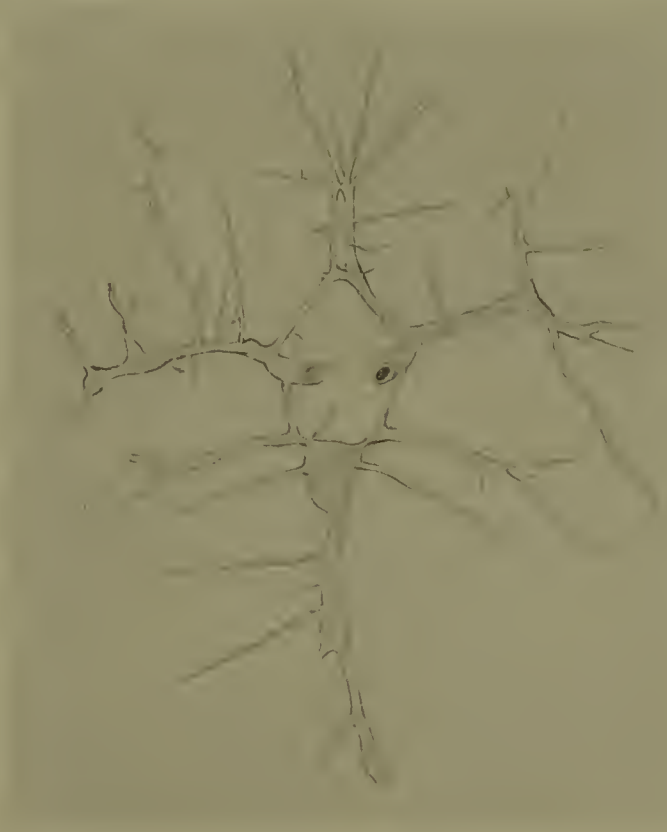

Fig. 2.—The circle of Willis and the larger branches of the cerebral arteries. Nat. size.

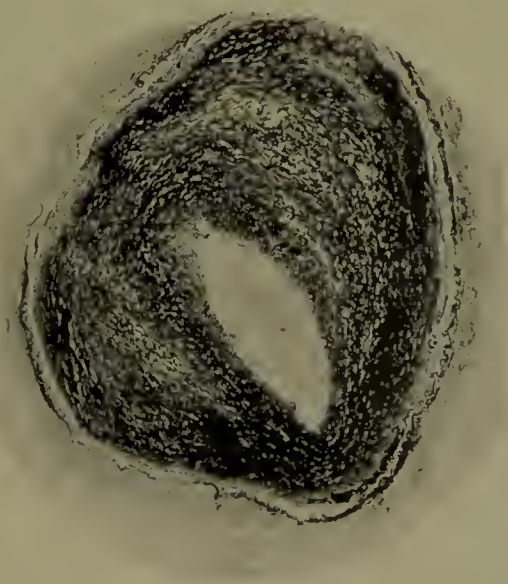

Fig. 3.—Transverse section of the right inferior cerebellar artery, showing great sub-endothelial overgrowth and imperfect elastic layer. Microphotograph.

was found filled with pale, laminated clot, which seemed to have occluded the entire lumen.

2. A slight fusiform dilatation exists at the hinder or lower end of the basilar, just after the vertebrals have united. Here the vessel measures 6 mm. across, as compared with 3 mm. where it enters the larger aneurysm described above.

3. A small fusiform dilatation on the left vertebral artery, the centre of which is 4 mm. across, and 1 in. below the upper termination of the artery.

4. A general distension of the coats of the left internal carotid artery from the point where it enters the cranial cavity to where the first vessels are given off. This is fusiform, and measures 6 mm. across. There is a slight general thickening around the whole circumference of the vessel walls, which are firm and rigid. The corresponding artery on the opposite side is also slightly dilated, but to a less degree.

5. A minute bulging on the right middle cerebral immediately after the anterior cerebral has been given off.

6. A dilatation at the origin of one of the branches of the same artery while in the sylvian fissure—probably the ascending frontal branch. The vessel is here 4 mm. across, compared to 2 mm., which would seem to be the natural diameter.

7. A small bulbous dilatation, 5 mm. across, at the fork between the two final main branches—probably the ascending parietal and the temporo-parietal branches.

8. A minute dilatation of the left anterior cerebral at its junction with the anterior communicating. At the site of 5, 6, and 7 the walls of the affected vessel are thickened, opaque, and hard, the lumen apparrently occluded by thrombi, and the circulation completely cut off.

After the brain had been preserved in formalin solution about three weeks, a more thorough examination was made. By carrying vertical transverse incisions through both hemispheres at intervals of about $\frac{1}{4}$ in., a number of areas of softening were found.

In the left cerebral hemisphere there was a small area about the size of a sago grain at the base of the calloso-marginal sulcus, on a vertical plane with the extreme anterior end of the genu of the corpus callosum. This involved both the grey cortex and the white matter. About half a dozen others were situated in the white matter of the occipital lobe and posterior part of the parietal of this hemisphere. These were all of small size, and, for the most part, of a triangular shape, the longest macroscopic measurement not extending more than $\frac{1}{3}$ in. They lay in the white matter, not far from the grey cortex, but not involving it. In most of these the softening immediately surrounded a somewhat dilated blood vessel. The basal ganglia in this hemisphere presented no visible lesion.

The right hemisphere contained no spots of softening in the hinder part. A section, immediately in front of the optic commissure, discloses an irregular cavity, $\frac{3}{4}$ in. vertically and $\frac{1}{4}$ in. across, situated in the outer part of the corpus striatum. This has been formed by the breaking down of the brain substance and, apparently, the softening of adventitious tissue. Part of the nucleus caudatus, the putamen of the nucleus lentieularis, and between these the internal capsule has been

entirely destroyed. By means of other sections it is found that this cavity extends in an antero-posterior direction for about ¾ in. In the fresh state the cavity seemed more ragged, and more or less filled with disintegrated tissue. The remainder of the grey matter of the lenticular nucleus (part of putamen and the globus pallidus) is pale and discoloured, and has a more yellowish tint than natural. The cavity is separated from the floor of the lateral ventricle only by a narrow intervening strip of brain tissue. In the upper and outer part of its side, there being no true wall, is a deposit of cheese-like substance of a yellow colour, which is believed to be of a gummatous nature. This substance is found to extend backwards beneath the floor of the ventricle for a distance of about ½ in. from the first section, and beyond the limit of the cavity; it expands in size, then separating into several foci which lie embedded in the brain tissue. A similar coloured mass is located at the lower extremity of the cavity. In a section on a level with the corpora albicantia there is found a small, oval, isolated cavity formed by softening in the white matter of the centrum ovale, rather above the level of the basal ganglia. It has a vertical length of a grain of wheat, but is a trifle broader. Sections through the right frontal lobe show this to be greatly disorganised. None of this change is visible on the surface of the brain, and does not involve the grey cortex. It is confined entirely to the white matter of the centrum ovale minor. A large irregular patch of softening has been formed in the lower portion, which extends pretty much over the whole extent of the orbital surface, with a vertical width varying from ¼ to ½ in. There is no true cavity, but the brain substance has disappeared in part, leaving a disintegrated and honeycombed appearance. There is a similar patch of smaller size beneath the cortex in the upper part of the lobe, below the superior and middle frontal convolutions and in front of the precentral sulcus.

The lobes of the cerebellum, examined with the same care, appear to be normal to the naked eye, except for a small area of softening in the region of the amygdala on the right side. This affected both the grey and white matter, and seemed to have caused a slight erosion of the surface of the restiform body immediately below the striæ medullares. Sections through the pons and medulla revealed no lesion. In connection with the patch of softening just referred to, it may be mentioned that the right inferior cerebellar artery, which was separated from the vessels about the circle of Willis on removal of the brain, was found to show marked signs of disease. There were a couple of distinct fusiform dilatations of its walls where the coats of the vessel were thickened and opaque. The lowest of these would about correspond to the seat of softening in the cerebellum.

Microscopical Examination, with Observations.—I am indebted to Dr. Watson for kindly preparing some excellent sections from several parts of the brain. These include the prefrontal region near the anterior extremity of the right frontal lobe, a part of the frontal lobe which includes the mesial and orbital cortex together with a part of the softened or gummatous tissue, and a section through the brain between the island of Reil and the lateral ventricle. In addition to these, he also prepared a transverse section of the trunk of the inferior cerebellar artery at the site of one of the thickenings. Sections from all these

sites have been stained by the polychrome-blue method to show the cell characters, and by the Heidenhain hæmatoxylin and eosin method more particularly to show the connective tissue and neuroglia formation.

The artery shows an advanced stage of endarteritis obliterans which at once stamps the case as syphilitic. Only the inner coat is affected. The lumen of the vessel is greatly reduced by a subendothelial proliferation which occurs around the whole circumference, though to an irregular extent. The deeper part (most external) of this tissue has undergone a hyaline degeneration. The elastic layer has disappeared in some places. This is well brought out in the hæmatoxylin-eosin section, where the elastic layer appears as a thin black streak (Plate IV., Fig. 3).

Sections of the frontal region, which include the covering pia mater, exhibit blood vessels with a variable degree of irregular subendothelial proliferation.

The cortex in the frontal region is reduced in width, and shows advanced acute and chronic degenerative changes of all forms of nerve cells, such as one finds in a typical case of general paralysis. The acute changes, Dr. Watson tells me, are the most marked in the polymorphous layer, while the chronic cell degeneration is the most conspicuous in the upper part of the pyramidal layer. There is also excessive neuroglia proliferation throughout the whole of the grey matter, but this is greatest in the molecular layer.

There is a proliferation of small blood vessels and capillaries; their number is much increased, and they exhibit certain abnormal conditions. The larger of these small vessels are dilated, and occasionally one may see a perivascular round-celled infiltration. But most interesting are the changes in the minute vessels. These consist of an endothelial proliferation and abundance of the so-called plasma cells on or composing their walls. Stained with polychrome-blue, endothelial cells take on a pale pink tint; but the plasma cells assume a mauvish-blue colour, and parts of the cell protoplasm, the outline of the nucleus, the nucleolus and chromatic strands are very deeply stained. The exact nature of the latter cells is still in doubt. By some they are believed to be of endothelial origin, while other observers think they are derived from lymphocytes. Dr. Mott at one time supported the first view, but more recently has altered his opinion and believes that "the balance of evidence is in favour of the plasma cells being derived from lymphocytes and not from endothelial cells" (1). For our own part, we believe the balance of evidence is in favour of the view that these cells spring from the lining endothelium of the small vessels and capillaries. But whatever be the origin of these cells, it has been said that they are rarely to be found except in some form of syphilitic brain disease, and more particularly in general paralysis of the insane. Some observers have gone so far as to look upon them as pathognomonic of this disease, in which they are mainly confined to the vessels of the fronto-central regions where in general paralysis the greatest wasting takes place. It may be noted, however, that recent observations do not altogether bear out such a sweeping statement. The existence of these cells in some non-syphilitic diseases has been conclusively proved, though it is true that this peculiar cell proliferation is most readily demonstrated in well-marked cases of dementia paralytica.

The cortex was examined in three places, namely, the extreme anterior frontal region, the mesial and orbital side of the same lobe, and the region of the insula. In all these parts the conditions above described may be seen.

In the grey matter of the corpus striatum and the white substance between this and the island of Reil, there is a more noticeable round cell infiltration around many of the rather larger vessels, which are often considerably dilated. Larger vessels still have a thickening of their muscular coat, and this has often undergone hyaline degeneration. One fair-sized vessel in this region shows an advanced stage of endarteritis obliterans.

Sections including two distinct patches of the honeycomb tissue in the white substance of the right frontal lobe prove that this is not merely softened and disintegrated brain substance but a new formation. There can be no doubt that this is syphilitic—a gummatous tissue which has undergone certain changes. The honeycomb structure is composed of trabeculæ of dense neuroglia, the intervening tissue having almost entirely disintegrated and disappeared. The peripheral portions of these bands of neuroglia are composed only of glia fibrils with an almost complete absence of nuclei; the central parts have much connective tissue nucleation, generally around small vessels which are more or less obliterated. These cells are partly the branching neuroglia cells, and are partly endothelial in origin. The absence of nuclei shows the gradual chronic cicatrisation and necrotic process that is taking place. The latter has already affected the intertrabecular tissue. The destructive process is least advanced at the edge of the slowly spreading growth. Here at the border, the brain tissue is inundated with numerous large branching glia cells, the so-called spider cells. These are evidently the precursors of a more dense fibrillar form of glia which goes to form the trabeculæ above referred to, while the enveloped portions of nerve substance, cut off from their blood supply, gradually undergo necrosis, and, by breaking down, ultimately leave the irregular cavities which produce the honeycomb appearance.

The process is identically the same as that which occurs in syphilitic gumma elsewhere, though there is here a greater tendency to the formation of cavities, owing no doubt to the want of a firmer external support. The ordinary connective-tissue proliferation which occurs in gummata in other organs and tissues is represented in the brain by glia proliferation, and the subsequent dense fibrosis and patchy necrosis which subsequently replaces the cellular element finds its counterpart in the more delicate fibrillar tissue of the neuroglia.

There is no reason to suppose that all the other areas referred to as softenings differed in any respects from those in the frontal lobe, for all, whether large or small, had the same naked-eye appearances. The larger the areas, however, the more extensive was the breaking down into cavity formation, as would naturally be expected in older and larger gummata.

It has been said that gummata of the brain are almost invariably situated superficially and connected with the pial covering or the processes of pia mater prolonged into the sulei; that

they are, more often than not, closely connected with one of the larger branches of the cerebral arteries. This is the view expressed by Gowers both in his "Manual of Diseases of the Nervous System" (2) and in his "Lettsomian Lectures" for 1890 (3). He says that almost the only place where they occur, strictly speaking, within the brain, is in the thalamic region, and there they are ingrowths from the side of the crus. W. A. Turner suggests much the same in his article on "Intracranial Syphilis" in Allbutt's "System of Medicine" (4). In the same volume Bullock (5) refers to Heubner as having found syphiloma in the interior of the brain only three times in forty-five cases.

My own previous experience as regards gummata of the brain was limited to those that have been superficially situated. Definite localised tumours, though embedded in the brain, were attached to the pia mater. I have recorded a good instance of this kind in the *Pathological Transactions* (6). Such localised tumours of syphilitic origin are very rarely found in the brain of persons who die insane, notwithstanding the fact that so many persons who die in lunatic asylums have a history of syphilitic infection. Areas of softening, on the other hand, are fairly common in the brains of lunatics, but are rarely examined microscopically. It is possible that some of these might prove to be breaking-down gummatous tissue.

From the microscopical characters of the tissue forming the breaking-down areas of softening in the present case, I have no doubt myself of its syphilitic nature. I attribute the difference in structure between the deposits in this case and that of a usually described gumma of the brain, to the fact that these were not directly connected with the pia or outer sheath of a larger vessel, and therefore the ordinary connective tissue is wanting and is represented by glia tissue. All the new tissue formations here have an irregular invading character without any distinct limitation or circumscribed tumour formation. The deposits are certainly not tubercle, nor are they gliomata, or any recognised form of malignant growth. They no doubt start from the smaller blood vessels within the brain substance, their connection with which is seen to be very intimate.

This hypothesis receives strong support from the microscopical appearances to be seen in parts of the brain where no softening or growth is visible to the naked eye. Around the vessels whose walls have undergone degeneration is a network structure formed by connective tissue or neuroglia cells. There can be no doubt that the large areas of disintegration commenced in a similar way. The surrounding brain tissue is altered from the normal. There is an unnatural fine fibrillary network pervading the whole structure, without, however, the actual disappearance of ground substance. The glia cells have assumed shapes and sizes which are not usually found in the normal white substance of the brain,

but which can readily explain the forms and varieties of cells to be found in the disintegrated areas of brain tissue.

Heubner recognises two characteristic forms of syphilitic growth in the brain—(1) A localised, firm, dry deposit, which on section is often found caseous and broken down in the centre, with a reddish and translucent periphery, and in which there is often much connective tissue developed. (2) An ill-defined, comparatively soft, moist, greyish or greyish-red mass, which on section exudes a scanty juice. The first of these is the variety that is generally recognised as gumma of the brain, and which occurs mostly at the base in the region of the larger vessels. The second form is that which occurs in the brain substance, and is generally believed to be very rare, but, as I have already remarked, it may be much more common than is generally supposed. The deposits I am now describing are evidently of this nature. As pointed out by Mills (7), gummata that develop in the substance of the brain originate from the vessels. This statement is borne out by the case now recorded.

General Remarks.—There are many features of more than usual interest presented by this case. The evidence of syphilis is undeniable. The mental disease of the patient during life presented the typical features of general paralysis of the insane, and the fatal malady ran a characteristic course, yet the brain presented an appearance more in accordance with gross syphilitic brain disease. The condition of the arteries, both large and small, stamps the disease as syphilitic even had a history been wanted, but this form of degeneration and subendothelial growth may occur in both diseases that have been named. It is, however, not usual to find areas of softening or gummatous tissue in the brain of general paralytics, at least to any extent. In this case they were numerous, and in places extending over a large area. Yet apart from these the histological structure of the brain is indistinguishable from that in dementia paralytica. There is the same form of cell degeneration, neuroglia proliferation, and changes in the small blood vessels. I have already commented at some length on the structure of the deposits that occur so numerously throughout both cerebral hemispheres, and have expressed the opinion that they are of gummatous nature, that is to say, syphilitic growths.

But the presence of gross syphilitic lesions in the brain, although rare in such cases, certainly cannot be said to nullify the clinical diagnosis of general paralysis. If general paralysis is a disease intimately associated with syphilis,—a purely syphilitic form of brain disease of a finer order, as some would have us believe,—the presence in the brain of a grosser form of syphilitic lesion is not to be wondered at. The strange thing, to my mind, is rather that gummatous deposits do not occur with greater frequency in this form of mental disease. Instead of annulling

general paralysis, such a case as this I consider tends to strengthen the syphilitic theory of general paralysis.

Many writers on general paralysis acknowledge that in a certain proportion of the cases of that disease, considerable difficulty may be experienced in differentiating from cerebral syphilis with a gross lesion. The discussion usually closes, however, with the statement that the discovery after death of a gummatous deposit clears up the diagnosis. On this point it is worth noting what Professor Ziehen of Berlin has to say. After writing of the differential diagnosis of cerebral syphilis and general paralysis, he remarks:

"It must be borne in mind that upon a circumscribed syphilitic focal affection (cerebral syphilis strictly so-called) a diffuse cortical alteration of the nature of dementia paralytica not infrequently supervenes; accordingly one observes clinically that to the uncomplicated symptoms of a syphiloma or gummatous meningitis there are added later the typical symptoms of a dementia paralytica: the brain syphilis has gone over into dementia paralytica. Finally, it must be taken into account that even anatomically from the beginning there exist transition forms between the diffuse paralytic cortical affection and the circumscribed gummatous infiltrations. Thus, even from the entire clinical course and post-mortem findings we shall not be able to make an absolutely sharp diagnosis in all cases" (8).

It is evident from the foregoing that Ziehen not merely recognises the difficulty of diagnosis between the two diseases, but that he goes further and states definitely that both gross syphilitic brain disease and general paralysis may coexist at the same time in the same individual. This is the view that I have ventured to assert, and it is satisfactory to find that so able an authority on the Continent holds views on the subject that may be regarded as identical with my own.

A case having many points of great similarity to the present one has lately been recorded by Dr. Emma W. Mooers (9). The paper is illustrated by diagrams showing the site of numerous focal lesions throughout the cerebral hemispheres. The sections of the brain seem to be studded over by necrotic areas, some of which were of considerable extent; for the most part they occur in the white matter, but some involve the cortex. The minute structure of these is thus described: "Thin sections from the various focal lesions were examined, and all show essentially the same histological structure, namely, masses of very cellular tissue enclosing foci of necrotic material. The cells making up the main masses consist of the various cells which may be found in granulation tissue and in lymphoid tissue. Interspersed among the cells are a large number of capillary blood vessels. The necrotic areas are generally seen to be bordered by elongated cells with vesicular nuclei and indefinite protoplasm (epithelioid cells). Giant cells

are occasionally found. In brief, the focal lesions have the general appearance of masses of granulation tissue undergoing necrosis, and have a structure which might be that of a gumma or a neoplasm due to tuberculosis, as we know of no purely histological criteria for distinguishing with certainty between the two diseases."

After pointing out the greater probability of these being syphilitic granulomatous new growths, the writer proceeds: "In the brain tissue adjacent to these focal lesions there is a well-marked increase in the neuroglia cells, some of which attain huge size. There is a replacement of brain substance in some regions by a spongy-looking tissue consisting of heavy bands of fibres, and, not numerous, but only loosely distributed among these, huge glia cells."

The patient, a man, æt. 40, was taken to the McLean Hospital because he presented certain symptoms which were thought to be evidence of general paralysis. Although the case is published as one of syphilis of the nervous system, the clinical history that is given is typical of general paralysis. He had a convulsive seizure about seven months before death, followed by other slight attacks, and the physical signs became more and more suggestive of progressive dementia paralytica. In addition to the gross lesions in the brain, there were marked lesions of a syphilitic nature found in the cord and its meninges.

Much difference of opinion still prevails, especially in this country, as to the relationship that exists between syphilis and aneurysmal disease of arteries. We see this strikingly brought out in Clifford Allbutt's "System of Medicine," published in 1900. In vol. vi. we find Dr. Mott expressing advanced views on the subject in his article on "Arterial Degenerations and Diseases." "I recall," he says, "very few cases of aneurysm of the aorta in men from whom I had not been able to obtain or detect a specific history. Likewise, a large proportion of cases of aneurysm of the cerebral arteries, and of the large vessels of the body, are of syphilitic origin" (p. 305). In the very next article on "Aneurysm of the Aorta," the subject of syphilis receives but scant notice from Dr. Gairdner. "Syphilis plays an important part in degenerative changes, which, however, are rather obstructive than aneurysmal" (p. 362). A remark made by Professor Drummond to the effect that he had found it a good practical rule not to diagnose aneurysm in a doubtful case, in the absence of syphilis, is labelled an "astonishing doctrine."

But the general question, whether or not syphilis is a common cause of aneurysmal dilatation of an artery, need not be now discussed; that syphilitic arteritis is sometimes the cause of aneurysmal dilatation can scarcely be said to admit of doubt. The present case is an instructive case from this point of view. Here we have a definite syphilitic disease of the arteries in a man not subject to any special strain on the vascular system, who

developed numerous aneurysms,—dilatations both on the thick-walled vessels of the neck and the thin-walled vessels in the cranium. The syphilitic disease of the arteries is unmistakable. The condition of the intima of the aorta is characteristic; it is very different to the ordinary atheroma. The character of the disease of the arteries of the brain, both external and internal, cannot be mistaken. There is no other disease which causes anything like this form of endarteritis obliterans. We may, I think, consider that syphilis was without any doubt the cause of the aneurysmal dilatations in this case.

Intracranial aneurysms have rarely in this country been attributed to syphilitic disease of the arteries. We could probably count the number of recorded cases on the fingers of one hand. Some writers on the Continent, however, are much more generous in the number of such aneurysms that they attribute to syphilitic disease. Gerhardt, in a lecture delivered in 1887 on diseases of the cerebral arteries ([10]), expressed the opinion that syphilis was a powerful factor in the causation of aneurysm of these vessels. In the present case there can be little doubt that the numerous dilatations on the large arteries at the base of the brain were due to local disease of the vessel walls. These vessels are evidently entirely obstructed in many places, so that no blood could pass. This is so of the basilar and the branches of the right middle cerebral. It was in the right cerebral hemisphere that the most extensive areas of softening were found, and the plugging of the branches of the middle cerebral artery of that side helps to explain the disintegrated condition of the white substance. These aneurysmal dilatations of the brain arteries were probably of quite recent origin; as aneurysms they produced no symptoms; they grew possibly with the accumulation and adhesion of clot and fibrin to the irregular lining of the diseased vessels.

Spontaneous aneurysm of the carotid artery does not rank among the most common of external aneurysms, but it is the most frequent of that class in the female. This is attributed to the fact that an aneurysm of this artery is seldom the result of violence or external strain, but generally arises from disease of the coats of the vessel. It also occurs at a relatively young age. These facts have been used as arguments in favour of syphilis as a factor in the causation of aneurysm. "The right carotid is much more commonly affected than the left, and the upper portion of the vessel than the lower; indeed, the bifurcation is the most common seat of aneurysmal dilatation" ([11]). In this situation they are usually of slow growth, and may sometimes exist for a considerable number of years without giving rise to any special inconvenience. They may, however, be of rapid growth, for Erichsen has seen a case of this kind attain the size of a small orange in a few weeks.

The occurrence of more than one aneurysm on the larger arterial trunks of the body is not common; two symmetrically situated aneurysms on the carotid arteries I have not seen described, and I do not think there is any specimen of this kind to be found in any pathological museum in London. The majority of recorded cases of multiple aneurysmal disease will be found, I believe, to be associated with ulcerative endocarditis or other acute infective processes, and are attributable to embolic origin. Many of the most interesting of these occurred in young persons.

In the present case the aneurysms do not appear to have been recognised during life, and it is impossible to say how long it had taken for them to acquire their size.

Aneurysm of the coronary arteries of the heart is certainly to be reckoned among the rarer pathological lesions. The condition is referred to in few text-books, in few even of the larger Systems of Medicine that have made their appearance in recent years. Comparatively few isolated cases appear to be recorded in medical literature. In comparison to this lesion, aneurysms of the heart and of the aorta in the region of the sinuses of Valsalva are fairly common, yet cases of both these conditions are constantly being recorded. This fact alone is sufficient, to my mind, to mark aneurysm of the coronary arteries as extremely rare, apart from the fact that with a large personal experience I have not previously seen a case of localised dilatation of these arteries such as would be defined as aneurysmal. Another condition, too, which has received a fair amount of attention, is narrowing or obstruction at, or near, the orifices of these arteries through degenerative conditions of their walls,—a lesion that can scarcely be looked upon as one of great rarity.

A search through that fruitful source of information, the *Trans. Path. Soc. London*, discloses the fact that only five cases of aneurysm of the coronary arteries appear to have been brought before the Society, and four of these were during the earlier years of its existence.

When, in January 1848, Peacock showed a specimen at the Pathological Society, he remarked "that the specimen exhibited was almost unique, no allusion being made to the occurrence of aneurysm of the coronary arteries by any of the systematic writers on pathological anatomy, or on diseases of the heart." He could only find the record of three cases, in each of which death resulted from rupture of the aneurysmal sac into the cavity of the pericardium, combined in one case "with rupture of the walls of the left ventricle, ascribed to the aneurysm having first burst into that cavity, and the rupture so formed being subsequently extended to the pericardium."

Subsequent cases have been recorded by Bristowe, Ward, and Crisp, and much more recently by Jackson Clarke. Crisp was able to collect twelve cases of aneurysm of the coronary artery

that he had met with in various museums and in the works of different authors, but he admits that only a few foreign journals were consulted. In commenting on these cases, Crisp observes: "It will be seen that, excluding my first case, which can scarcely be called one of genuine aneurysm, all the eleven subjects of this lesion were males, and that in seven examples the aneurysm ruptured into the pericardium. As might be expected, in no instance was the presence of this aneurysm suspected during life." Without attempting to search further into medical literature,[1] we have here, I think, sufficient evidence that aneurysms of the coronary arteries are rare; that when they do occur they may be solitary, but almost as frequently they are multiple; that more often than not their rupture is the immediate cause of death; and that the origin of these aneurysms is usually to be attributed either to embolic plugging of the vessel or to syphilitic disease of its wall. Although the latter disease is not stated to have been present in either of the above cases, there is little doubt in my own mind that it was present in more than one instance.

Since the foregoing was written, I find that the subject of aneurysm of the coronary arteries of the heart has been dealt with far more fully than previously by Wardrop Griffith in a paper brought before the Leeds and West Riding Medico-Chirurgical Society, and printed in the *Brit. Med. Journ.*, London ([12]). Having noted the fact that aneurysmal dilatation of these arteries is "so uncommon," he proceeds to record two cases, both of which would seem to be of embolic origin, secondary to acute infective endocarditis.

A considerable part of Griffith's paper is taken up with a general discussion on embolism and its relation to aneurysm of the smaller arteries. He has, however, been at considerable pains to look up the literature bearing on aneurysm of the coronary arteries. He discards several of the examples mentioned in the primary references as probably not coming within the category of true aneurysms of these arteries. Excluding the doubtful cases, there remain, with his own, twenty-four examples published between the years 1812 and 1900 ([13]). In six of these, few particulars are given; in exactly half of the remaining eighteen, death occurred from rupture into the pericardial sac.

"In eleven instances the aneurysm was solitary, occurring four times on the right and four times on the left artery, while in three instances its situation is not noted. In the seven instances in which the aneurysms were multiple, they varied in number from three up to twelve. In only two instances is it noted that the aneuryism was in the auricular wall; in all the others it appears to have been on the main stem of the artery, or on the ventricular

[1] It may be noted, however, that reference to the indices of the *Brit. Med. Journ.*, London, and its "Epitome of Current Medical Literature," for the last ten years, failed to reveal a single case beyond those contained in Griffith's paper.

part of the heart, and usually on the latter. Some writers who mention the site state that the aneurysms were at or close to the points of origin of branches, a fact of some importance in relation to causation. In size they have varied from that of a chestnut to that of a small pea. In fourteen instances the affection occurred in the male sex, and in four in the female. Of the fourteen instances in which the age is noted only five were above the age of 26, and the ages varied from 5 to 77."

In discussing the causation of these aneurysms, Griffith refers only to the embolic theory as applied to a certain proportion of the cases. He is able to say that in only four of the eighteen cases could this mode of origin be regarded as certain. These four cases included his own two cases and those recorded by Bougon and Ogle. Of Bougon's case, however, he notes that "the patient was an old man, and the coronary arteries were studded with osseous plates." Ogle in his paper in the *St. George's Hosp. Rep.* for 1867, London, was the first writer who definitely attributed coronary aneurysm to embolism. His former case, published in 1864, may have illustrated the very commencement of an aneurysm due to a similar cause. Embolism is looked upon as highly probable in Clarke's case, and also in Bristowe's case, for although in the latter case the cardiac valves were said to have been healthy, yet the internal organs contained embolic infarcts. The cases of Peacock, Heuse, Crisp, Peste, Gee (æt. 7), Malet and Evans (æt. 5), the Bartholomew's Hospital case (æt. 11), and that of St. Thomas's Hospital (æt. 22), are also looked upon by this author as probably due to embolism; but it seems to me that the attempt to class some of these under an allied etiology is made on very weak and insufficient evidence. In the cases of Markoe, Wood, Hedland, and Merat, Griffith acknowledges that he can find no facts on which to form an opinion.

The possibility of syphilitic disease of the artery as a cause of the affection does not appear to have entered into the calculations of this writer, for no reference whatever is made to the subject. This is the greater pity, for it is evident that much time has been expended on looking over the original records.

The author concludes his remarks by saying: "I have intentionally refrained from any attempt to discuss the clinical phenomena of coronary aneurysm. The symptoms are, with the exception of those caused by rupture, chiefly those of the associated condition. The affection might be guessed at, but hardly, I think, diagnosed, and the two chief points I desire to emphasise are, the rarity of its occurrence, and the probability of its sharing the peculiarity of aneurysms on small vessels elsewhere, in being embolic in origin."

As already observed, there is little or nothing said on coronary aneurysms in medical works of the present day; this circumstance, in conjunction with the views expressed by Griffith, who would

seem to assign all to an acute infective embolic origin, must be my excuse for entering somewhat fully on the subject in these pages.

Pepper's "System of Medicine" is to some extent an exception to both these remarks, for Cutler (14) in a short section on this condition, while referring to the rare occurrence of aneurysm of the coronary arteries, says the most common cause of the affection is chronic endarteritis, where, through disease of the intima, the resistance of the blood pressure is diminished; while embolism is another, though rarer, cause. He further notes that aneurysms on this vessel are rarely larger than a pea, and that the termination is usually rupture with fatal hæmorrhage, in far the majority of cases into the pericardium. "In almost all the cases I have found recorded there were no symptoms till rupture of the sac occurred, giving rise to death from hæmorrhage. Then those symptoms which might be expected occurred, namely, great præcordial pain, dyspnœa, suffocation, tumultuous heart, irregular and intermittent pulse, and sudden death." Syphilitic arteritis of the coronary arteries more frequently manifests itself by a constriction of the lumen of the artery than by a dilatation, and it is not at all rare to find a considerable obstruction to the orifice of these vessels when syphilitic aortitis is present. That condition more often than not seems to commence about the sinuses of Valsalva.

Thrombosis of the coronary arteries is probably a good deal more frequent than is commonly supposed, but it is generally recognised that embolism of these arteries is extremely rare. Welch (15) points out that while arterial thrombosis may be caused by some local injury or disease of the arterial wall or by the lodgment of an embolus, that of the coronary arteries is in the great majority of cases an incident of angio-sclerosis of the heart. "It may also result from acute or chronic endaortitis near the orifices of these arteries, and possibly from acute inflammation of the coronary arteries. Thrombotic vegetations, springing from the aortic valves, have been known to block the mouth of one of the coronary arteries." The anastomoses that occur between the larger trunks do not usually suffice for the nutrition of the heart after rapid occlusion either of the main trunks or of intramuscular branches. Mott (16) observes that syphilitic arteritis of these arteries may be followed by thrombosis. This may cause necrotic patches in the myocardium. "The degenerated tissue may yield, and an aneurysm of the heart result; but more commonly there is a gradual process of coagulum necrosis of the muscles and fibrous substitution, thus accounting for many cases of the so-called fibroid heart of syphilitic origin." Cases of almost complete obstruction are generally rapidly fatal.

A heart from a case of angina pectoris was shown at the Pathological Society by Parkes Weber (17), in which the channel of the right coronary artery was obliterated by organised thrombus at about $2\frac{1}{2}$ in. from its orifice for a space of about 1 in. The

lumen of the left coronary artery was also much narrowed by atheromatous changes at about 2 in. from the orifice. The heart was in a state of extreme fibroid degeneration. The patient had pulmonary tuberculosis, and died during an attack of angina at the age of 56. No mention is made of syphilis. Barth ([18]) has reported the case of a young man of 30, who died suddenly when in apparently the best of health. The orifice of the right coronary artery was found blocked by a thrombus attached to a small atheromatous patch in the aortic intima. This was the only patch of atheroma that could be found in what otherwise seemed a perfectly healthy body. Sudden death has also been recorded where an embolus has lodged in the main trunk of one of these arteries. Such a case is recorded by Cyril Ogle ([19]). A youth, æt. 17, suddenly became very distressed for breath, and cyanosed, and died within ten minutes of the onset of the symptoms. Here, one of the main divisions of the left coronary was firmly plugged by an embolism derived from a polypoid mass in the left ventricle.

Death may, however, occur with equal suddenness when the obstruction to the flow of blood through these arteries is due to other causes. Thus in a case recorded by Samuel West ([20]), a man of about 40 died suddenly while in hospital for heart disease. In this case the mouth of the left coronary artery was completely obliterated by a calcareous plate, though the vessel was pervious and of normal size beyond the obstruction. The right coronary artery was large, but its mouth considerably narrowed by atheroma.

There are, however, plenty of other cases on record where the main trunk of one of the coronary arteries has been plugged without the occurrence of sudden death. In such cases the patients have gradually sunk from cardiac failure in the course of a few days after the obstruction. The symptoms resulting from coronary thrombosis are indistinguishable from those of advanced fibroid disease of the heart, and may occur in cases of sclerosis of the coronary arteries without thrombosis, so that it is not possible to make a diagnosis of thrombotic occlusion. It is possible that the latter condition was the immediate cause of death in the case which is the subject of this paper.

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14. Pepper.—"System of Medicine," 1885, vol. iii. p. 830. 15. Allbutt.—"System of Medicine," vol. vi. p. 208. 16. Allbutt.—"System of Medicine," vol. vi. p. 314. 17. *Trans. Path. Soc. London*, 1896, p. 14. 18. *Deutsche med. Wchnschr.*, 1896, p. 269. 19. *Trans. Path. Soc. London*, 1896, vol. xlvii. p. 29. 20. *Idem*, 1883, vol. xxxiv. p. 66.

Note.—The following are the twenty-four cases of true coronary aneurysm given by Griffith, arranged in chronological order. The six marked (*) are excluded from that writer's summary, owing to want of particulars :—

Bougon.—*Bibliothèque Méd.*, 1812, p. 37. *Wiegaud.—*Med. Convers. Bl. Hildburgh*, 1830, p. 217. Peste.—*Arch. gén. de méd.*, Paris, 1843, vol. ii. p. 274. Merat.—*Dict. des Sciences méd.*, 1849, vol. v. p. 484. Hedland.—"Otto's Compendium of Patholog. Anatomy," 1849. Peacock.—*Trans. Path. Soc. London*, 1849, vol. i. p. 227; *Monthly Journ. Med. Sc.*, 1849, vol. ix. p. 592. Heuse.—*Presse méd. belge*, Bruxelles, 1856. *Finnell.—*New York Med. Journ.*, N.S., 1856, vol. xvi. p. 82. Bristowe.—*Trans. Path. Soc. London*, 1856, vol. vii. p. 98. Wood.—Quoted by Ogle, 1860. Markoe.—*Idem.* *Shrady.—*New York Med. Press*, N.S., 1860, vol. iii. p. 225; *New York Med. Journ.*, Ser. 3, 1860, vol. viii. p. 384. *Chadwick (2 cases).—Referred to by Ogle, 1867. Ogle.—*St. George's Hosp. Rep.*, London, 1867, vol. ii. p. 285. *Buchner.—"Aneurysma der Arteria Coronaria Cordis Sinistra," Amsterdam, 1867.—Bart.'s Hosp.—Referred to by Crisp, 1871. Bart.'s Hosp. and Gee.—*St. Barth. Hosp. Rep.*, London, 1871, vol. vii. p. 148. Crisp.—*Trans. Path. Soc. London*, 1871, vol. xxii. pp. 106–111, with table. St. Thomas's Hosp.—Powell in "Reynold's System," 1879, vol. v. p. 132. Malet and Evans.—*Lancet*, London, 1887, vol. ii. p. 67. Clarke.—*Trans. Path. Soc. London*, 1896, vol. xlvii. p. 24. Griffith (2 cases).